UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Marianne Lewis

From: Matthew Aubuchon, Ph.D., Entomologist

Secondary Review: Jennifer Saunders, Ph.D., Senior Biologist

Date: 4/26/2017

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER DOES NOT CONTAIN CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 438756
Decision no.: 525066
Submission no: 996875
Action code: R340
Product Name: IMI-Lambda Granular T&O Insecticide
EPA Reg. No or File Symbol: 228-610
Formulation Type: Granular
Ingredients statement from the label with PC codes included:

lambda-Cyhalothrin	0.04%	PC: 128897
Imidacloprid	0.2%	PC: 129099

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m$_2$ or mg/cm$_2$ or mg/kg body weight as appropriate): Granular formulation applied between 2-4.6 lbs / 1000ft^2 (0.998 – 2.088 g a.i. / 1000 ft^2). Specific rates are denoted for turfgrass, ornamentals, and flower beds.

Use Patterns: Outdoor use around buildings, lawns, base of ornamental trees and shrubs, parks, recreational areas, and athletic fields. May be applied around public, industrial, residential, and commercial structures.

I. Action Requested: Efficacy review requested for MRID 50136301 to determine if efficacy claims against fleas, ticks, and red imported fire ants are supported.

II. Background: Product specific data were submitted by the registrant to support the addition of fleas, ticks, and red imported fire ants to this product.

III. MRID SUMMARY 50136301

Fleas *Ctenocephalides felis*

(1). Non-GLP

(2). Methods: Separate strips of fescue sod were placed in plastic bins and treated with subject product 228-610 at a rate of 1g / $1ft^2$. Tested rates correspond to the lowest approved labeled rate. Six individual disks (4" diameter) were cut from treated sod and untreated sod strips (12 total) and placed into 1.2-pint mason jars. Sod discs were inserted such that fleas had only a few centimeters of space above the treated sod to move. Ten (10) adult fleas were placed into each of the jar arenas and exposed to the treatment for 24 hrs. Test intervals were conducted as follows: pre-treatment, then 3 d, 7 d, 14 d, and 21 d post treatment. At each time interval, a new batch of fleas purchased from a biological supplier was introduced to the aged treatments. Test authors noted that five arenas were evaluated per treatment for 7 d evaluations due to a shortage of fleas. Endpoints for tests included knockdown and mortality of fleas. Authors analyzed data with the non-parametric Wilcoxon test.

(3). Results: Reported graphical representations of the data suggested that an average of 90% flea mortality in treatments at 14 d and 21 d post treatment. Reported mortality at 3 d and 7 d post treatment was below the 90% efficacy threshold. Mortality of fleas within the controls was reported as <10% at 3, 7, 14, and 21 days post treatment.

(4). Conclusion: This flea study is unacceptable and does not support that the subject product 228-610 controls fleas at the rate of 1g / $1ft^2$ applied in a lawn environment.

Fleas were exposed to the treatment for a period of 24 h. This long exposure scenario is not realistic given the nature of how granular formulations will work in the field.

Metrics of mortality and knockdown or "intoxication" as stated in the report were discussed, but neither of these metrics were disclosed separately. Because the raw data were not included, the reviewer has no way of determining if reported results separated mortality from knockdown. Therefore, the reviewer must assume both metrics are combined. This is unacceptable since combining these metrics inflates the reported mortality.

Unnecessary statistical methods obfuscated the results of this study. The use of a Wilcoxon test (non-parametric two-sample test) was unjustified and unnecessary. If a researcher chooses to use non-parametric instead of parametric analyses, then a statement regarding the distribution and/or variance within the data set would assist the reviewers. No such statement about the data was included. The graphical representations along with the results/discussion referenced the mean flea mortality; the Wilcoxon results tables highlighted means and standard errors. Considering that non-parametric analyses test hypotheses based upon the median, references to arithmetic means and standard errors did not appropriately connect results with the analysis.

None of these reported statistical methods clearly disclose whether or not the product applied at the lowest labeled rate achieves a 90% mortality level in fleas. When reviewing the reported "means" in the Wilcoxon tables, it is clear to the reviewer that efficacy was well below the 90% threshold with broad variation across the results. If the reported numbers were in fact mislabeled medians, then the results of the reviewer's conclusions still hold.

Ticks *Rhipicephalus sanguineus*

(1). Non-GLP

(2). Methods: Separate strips of fescue sod were placed in plastic bins and treated with subject product 228-610 at a rate of 1g / $1ft^2$. Tested rates correspond to the lowest approved labeled rate. Six individual disks (4" diameter) were cut from treated sod and untreated sod strips (12 total) and placed into 1.2-pint mason jars. Sod discs were inserted such that ticks had only a few centimeters of space above the treated sod to move. Ten (10) adult dog ticks were placed into each of the jar arenas and exposed to the treatment for 24 hrs. Test intervals were

conducted as follows: pre-treatment, then 3 d, 7 d, 14 d, and 21 d post treatment. At each time interval, a new batch of ticks purchased from a biological supplier was introduced to the aged treatments. Endpoints for tests included knockdown and mortality of ticks. Authors analyzed data with the non-parametric Wilcoxon test.

(3). Results: Reported graphical representations of the data suggested that an average of 90% tick mortality in treatments at 3 d and 7 d post treatment. Reported efficacy dipped below 90% for times 14 d and 21 d post treatment. Control mortality was reported as <10% for 3 d, 7 d, 14 d, and 21 d post treatment.

(4). Conclusion: This study does not support that the subject product 228-610 controls ticks at either rate in a lawn environment.

Ticks were exposed to the treatment for a period of 24 h. This long exposure scenario is not realistic given the nature of how granular formulations will work in the field. Qualitative observations by the authors noted possible repellent behaviors exhibited by ticks in the treated jars. If the material is in fact repellent to ticks, then it stands to reason they would move away from the treated area in the field, further compressing their exposure time. Furthermore, metrics of mortality and knockdown were collected but neither of these metrics were disclosed separately. Because the raw data were not included, the reviewer has no way of determining if reported results separated mortality from knockdown. Therefore, the reviewer must assume both metrics are combined. This is unacceptable since combining these metrics inflates the reported mortality, especially for 3 d and 7 d post treatment where tick mortality was reported as >90%.

Unnecessary statistical methods obfuscated the results of this study. The use of a Wilcoxon test (non-parametric two-sample test) was unjustified and unnecessary. If a researcher chooses to use non-parametric analyses instead of parametric analyses, then a statement regarding the distribution and/or variance within the data set would assist the reviewers. No such statement about the data was included. The graphical representations along with the results/discussion referenced the mean tick mortality and the Wilcoxon results tables highlighted means and standard errors. Considering that non-parametric analyses test hypotheses based upon the median, references to arithmetic means and standard errors did not appropriately connect results with the analysis.

Red Imported Fire Ants (RIFA) *Solenopsis invicta*

Broadcast and mound-drench applications against RIFA were conducted in Texas, Georgia, and Florida.

Texas

(1). Non-GLP

(2). Methods: *Mound Treatments* – Eight (8) plots (4 treated; 4 untreated) containing 10 active RIFA mounds within each plot area were designated. One half cup (227 g) of subject product 228-610 granules was sprinkled over each mound plus a 2-ft. radius around each mound. Granules were watered in using 1.5 gal of water.

Broadcast Treatments - Twelve plots measuring 100 ft. x 100 ft. were delineated, each with 10 active RIFA mounds. Study consisted of three (3) treatments with four (4) replications per treatment. Plots were blocked in ordinal fashion from highest to lowest number of fire ant mounds per plot. Replications were established by dividing the array into four blocks and randomly assigning the 3 treatments to plots within each block to ensure that pre-treatment mean differences among all treatment blocks was minimal. Applications were conducted with a walk-behind spreader; treatments consisted of 2 lb. / 1000 ft^2,3 lb. / 1000ft^2, and untreated controls. All plots were watered with 175 gallons of water applied with a high-volume sprayer. RIFA activity was monitored pre-treatment, then at 14, 30, and 60 d post treatment.

(3). Results: *Mound treatments* - Reported reduction in activity was reduced to 85% at 14 d post treatment; graphical representation depicted approximately 90% reduction of mounds at 14 d post treatment. Reduction of RIFA activity was significantly lower than the control at 14 d and 30 d post treatment, but the quantified reduction in activity in the treatment seemed to be masked by reduction of activity in the controls. See "Figure 3" extracted from study for graphical display of results.

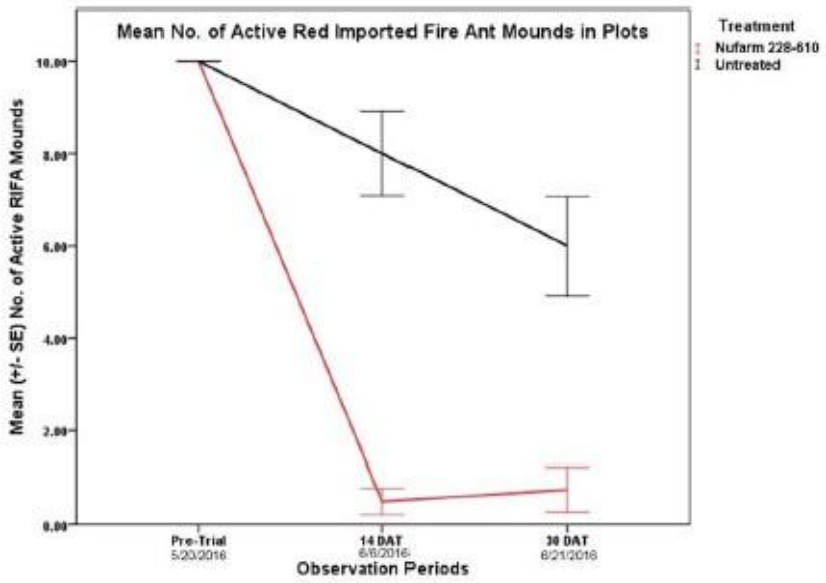

Figure 3: Mean (+SE) number of active fire ant (RIFA) mounds within plots at pre-trial (5/20/2016), 14 (6/6/2016) and 30 (6/21/2016) days after treatment (DAT). Student's t-test was used to analyze data. Significant differences occurred when P<0.05. College Station, Brazos County, TX, 2016.

Broadcast treatments – RIFA activity declined numerically at 14 and 30 d post treatment but not significantly until 60 d post treatment. The low rate of 2lbs / 1000ft^2 reduced RIFA activity by 40%; the higher rate of 3 lbs / 1000ft^2 reduced RIFA activity by 60% at 60 d post treatment. See "Figure 5" extracted from study for graphical display of results.

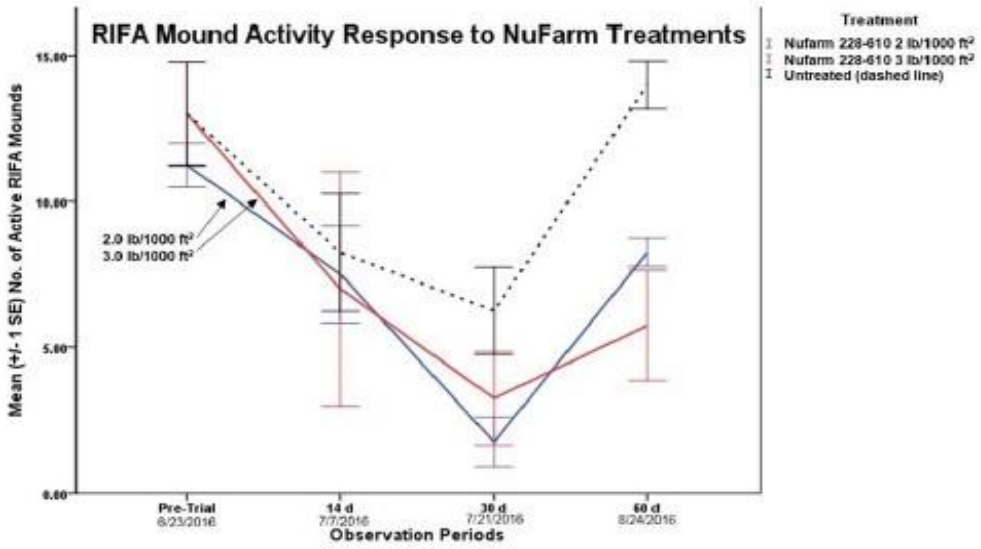

Figure 5: Mean (+ SE) number of active fire ant (RIFA) mounds observed during pre-trial, 14, 30, and 60 days after treatment (d) observation periods. Data was analyzed via Analysis of Variance (ANOVA) at P < 0.05 and means separated using Tukey's HSD (Honest Significant Difference) test at P< 0.05 (SPSS for Windows, V. 22.0). Significant differences occurred when P<0.05. College Station, Brazos County, TX, 2016

(4). Conclusion*:* When applied as a mound drench or broadcast, this study does not support that the subject product 228-610 controls fire ants by 14 d and 30 d post treatment in TX. In mound drenches, average levels of RIFA activity dropped by 20% in the untreated controls by 14 d, then continued to drop by 30 d post treatment. Although the reviewer acknowledges that the reduction in mound activity was significantly lower than the untreated control, the 1-way ANOVA did not account for the changes in activity through time. For broadcast applications, RIFA activity level mirrored the treated controls such that there were no significant differences among all of the plots for up to 30 d post treatment (Figure 5). Between 30 and 60 d, RIFA activity increased within and among all plots. Although treated plots were significantly different from the untreated controls, the subject product 228-610 was not efficacious at or near 90%. Study authors noted that increased rainfall may have accounted for these increases in RIFA activity stemming from new establishing mounds (Figure 5).

A two-way repeated-measures ANOVA or a Mixed-Model may provide appropriate adjustments for field studies conducted over time, however the reviewer advises that researchers consult a statistician for best analysis. Based upon the data, the reviewer cannot determine if the reduction in activity was due to the treatment or other environmental factors.

Georgia

(1). Non-GLP

(2). Methods: *Mound Treatments* – Six (6) plots (3 treated; 3 untreated) were containing 10 active RIFA mounds within each plot area were designated in a Random Complete Block Design. One half cup (227 g) of subject product 228-610 granules was sprinkled over each mound plus a 2-ft. radius around each mound. Granules were watered into each mound using 1.0 gal of water.

Broadcast Treatments - Six plots, each with 10 active RIFA mounds were designated with consisted of two treatments (application rates) and three (3) replications per treatment. The subject product was applied at rates of 2 lb. / 1000 ft^2 and 3.4 lb. / 1000ft^2 using a hand-shaker applicator. Plots were arranged in a Randomized Complete Block. No untreated control was specifically designated for broadcast plots and plot sizes were not disclosed. All plots were lightly watered after initial application, then an irrigation system delivered additional water to the plots over the course of 82 d. RIFA activity was monitored pre-treatment, then at 15, 30, 45, 60, 75, and 80 d post treatment. Author noted that broadcast applications were repeated approximately five weeks into the study due to low efficacy.

(3). Results: *Mound Treatments* – RIFA activity decreased by 40% at 15 d and 100% by 30 d post treatment. Activity remained at 100% within treated mounds for the duration of the study (60 d). Control performance was acceptable with <10% RIFA mortality across all observation times.

Broadcast Treatments – Reported efficacy for both application rates did not exceed 64%. A second treatment was conducted and reported efficacy numbers increased to 100% by 75 and 82 d post treatment.

(4). Conclusion: This study does not support that mound drenches and broadcast applications of the subject product 228-610 controls RIFA. Mound drench applications are intended for targeted elimination of individual mounds within a short period of time. Usually these targeted applications are reserved for sensitive areas where RIFA pose a significant stinging threat towards people. The submitted data demonstrated that mound drench applications needed almost one month before they demonstrated efficacy above 90%. It is the reviewer's opinion that this time period is too long for this formulation to act. The broadcast applications at the low and high rates did not achieve efficacy above 90% for 60 d after the initial application. A second application was conducted around 60 d post treatment, but the treatment clock was not reset. Therefore, the 75 d and 82 d efficacy of 100% does not reflect true results because the initial application already reduced RIFA activity 46-64% during the first 60 d. The reviewers have no way of determining if the exposure to RIFA from both treatments corresponds to the rates tested.

In the methods, the authors described their experimental design as a Randomized Complete Block, but they did not define their blocking factor nor did they define a corresponding statistical analysis to accompany that blocking factor. Reviewers were confused why these items were mentioned since the data summary consisted of descriptive statistics.

Florida

(1). Non-GLP

(2). Methods: *Mound Treatments* – No individual mound drenches were conducted with the test product Protego Plus Fertilizer 0-0-7 (NUP-16025: 0.2% imidacloprid; 0.04% lambda-cyahalothrin).

Broadcast Treatments - Seven plots measuring 5000 ft^2 were delineated, each with 10 active RIFA mounds. Study consisted of two (2) treatments with three (3) replications per treatment plus one (1) untreated control plot. Experimental design did not have replicates for untreated controls. Applications were conducted with a walk-behind spreader; treatments listed as 2 oz. / 1000 ft^2 and 3.3 oz. / 1000ft^2. Reviewer notes that rates were reported in oz. / 1000 ft^2 instead of lbs. of product / 1000ft^2. A subsequent watering plan was not disclosed.

The endpoint for broadcast consisted of "aggregate totals" of active living fire ants emerging from the mounds when disturbed with a wire.

(3). Results: Highest level of efficacy was reported at 72.9% reduction in active living fire ants. Control performance was acceptable with RIFA mortality <10% throughout the study.

(4). Conclusion: This study does not support that the subject product 228-610 controls RIFA. Methods for counting active fire ants emerging from a disturbed mound are not disclosed. The reviewer has concerns about the accuracy and reproducibility of counting active fire ants in the field. Fire ants quickly emerge from disturbed nests, ascend grass blades, and expand in all directions beyond the mound perimeter. Reliable methods for RIFA activity that do not excite their alarm response are in the published scientific literature. More importantly, published methods are reproducible and seek to mitigate sampling error. Initially, study plots were established based upon area and number of active mounds (10). Using active mounds as the designated endpoint, RIFA activity ceased in 9 mounds out of 60 treatment mounds. These results are below the 90% efficacy threshold.

IV. EXECUTIVE SUMMARY

MRID 51036301 is **unacceptable**. Product 228-610 did not demonstrate sufficient efficacy against fleas, ticks, and fire ants. Submitted studies had incorrect statistical analyses and demonstrated declines >10% within the controls. Reviewer could not distinguish between mortality and knockdown, and no raw data were submitted to clarify data metrics.

V. LABEL RECOMMENDATIONS

(1) Make the following changes to the Directions for Use:

- Efficacy data do not support addition of fleas, ticks, and RIFA to DFU

(2) The following marketing claims are acceptable: Current qualifications on the label indicating that 228-610 is not for use against carpenter ants, pharaoh ants, fire ants, and harvester ants.

(3) The following marketing claims are unacceptable: Adding kills and control claims against fleas, ticks, and fire ants are unacceptable.

(4) The following MRIDs should be removed from the data matrix, as they are classified as "**unacceptable**" to support the product: 51036301